



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

19 December 2011
EMA/733642/2011
Human Medicines Development and Evaluation

Outcome of SME office survey on the implementation of the SME regulation - Commission Regulation (EC) No 2049/2005

1. Background, objectives and scope of the survey

With the aim of promoting innovation and the development of new medicinal products by SMEs, Commission Regulation (EC) No 2049/2005 ('The SME Regulation'), implementing provisions relating to SMEs in the EU pharmaceutical legislation¹, was adopted on 15 December 2005.

The Agency is required to report annually on the operation of the SME provisions laid down in the SME regulation, so that feedback on their practical application is available.

The objective of the SME office survey, launched in March 2011, was to receive detailed feedback from SMEs and their stakeholders on the SME initiative 5 years following its implementation.

It also aimed to gather information on how successful (or not) the measures introduced to support SMEs have been, and to identify current and future challenges faced by SMEs in the pharmaceutical sector.

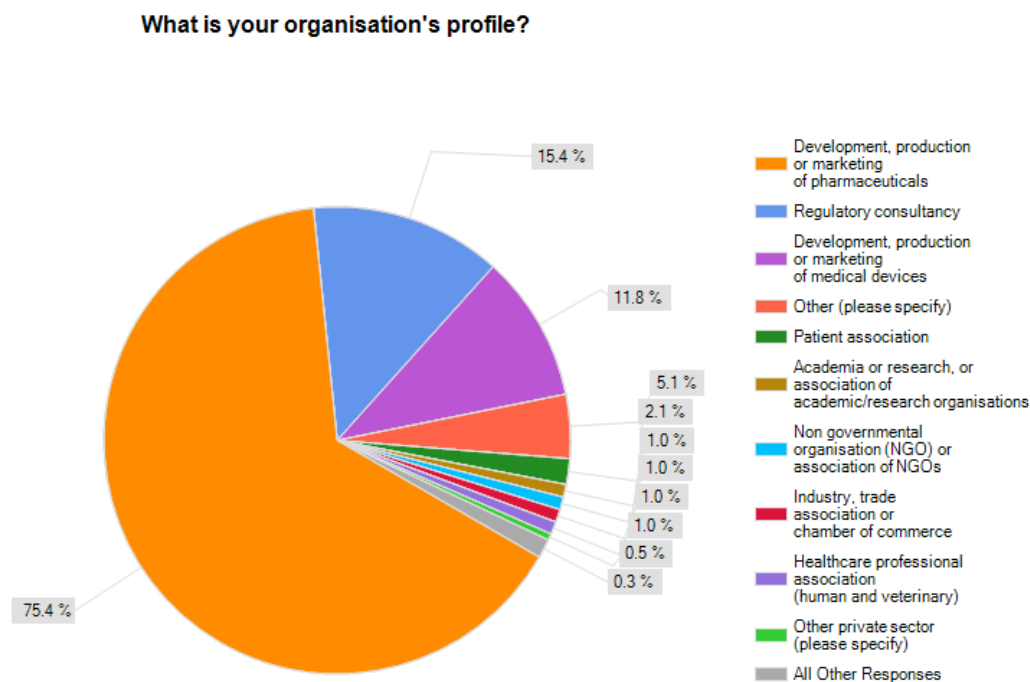
The consultation took place over a 4 week period through a web-based survey. It was published on the EMA website on 24 March 2011 and was sent via e-mail to contacts from the SME database (1013 records) as well as all SME-specific stakeholders.

¹ European Parliament and Council Regulation (EC) No 726/2004 of 31 March 2004



2. Profile of respondents

Two hundred and sixty-three (263) responses were received. Of those, 222 responses were considered as valid (answering at least the first 4 questions of the questionnaire). The majority of responses (78%) originated from registered SMEs, 10% were completed on behalf of organizations and 12% by individuals. The field of activity of the respondents was in human health (80%), veterinary (10%) and both (9%). The business activity of the majority of companies was pharmaceuticals (75%), 12% were in the medical device field and 15% were regulatory consultancies.



Profile of respondent SMEs

The questionnaire was anonymised with the option for respondents to provide details about the name of the company and the contact details. Of those respondents providing this information, 85% (68) were companies registered by the EMA.

The profile of the respondent SMEs was as follows:

- The majority are based in the UK, Germany or France.
- 49% are micro-, 33% small- and 18% medium-sized.
- 73% in the human health field.
- 88% are (bio)pharmaceutical enterprises developing therapeutic medicines (87%), 12% are companies in the medical device sector.
- 37% are development stage companies and 27% are at the research/discovery stage.

- 25% are academic spin offs.
- The profile of shareholders is spread between a) individual private investor (48%) mainly held by investor founders and employees/directors; b) corporate ownership (42%) mainly held by venture capital companies; c) public bodies (6%) mainly held by regional development funds and d) foundations (4%).

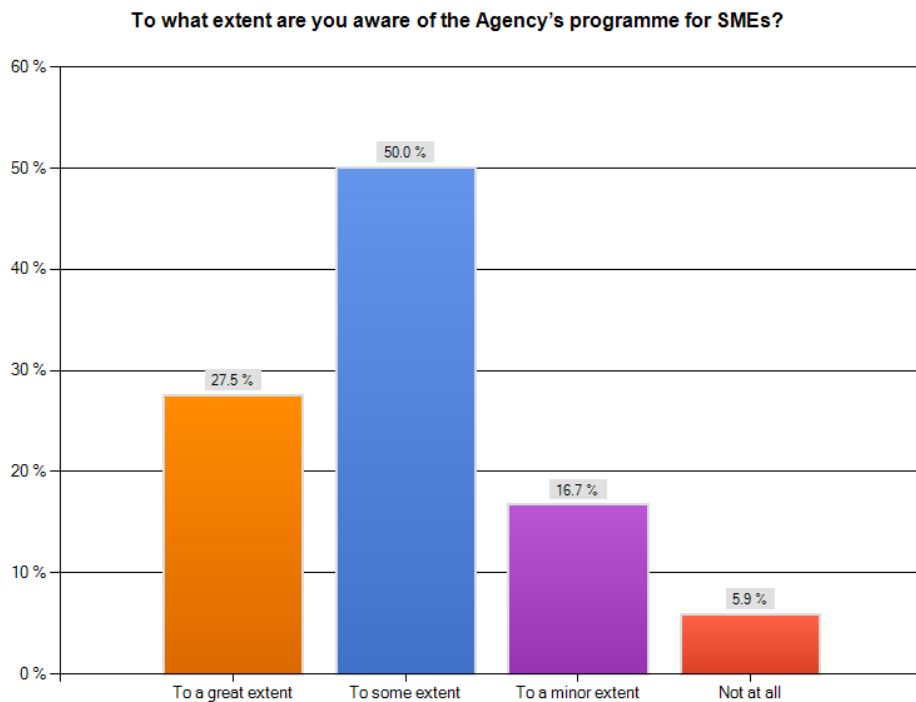
The product pipelines include chemicals (33%), biologicals (23%) and advanced therapies (14%). These products are at the research/discovery stage (17%), pharmaceutical development stage (17%), preclinical stage (19%) exploratory clinical stage (15%), confirmatory clinical stage (11%), (pre)registration (12%), marketing stage (9%). A third of these products are developed in orphan conditions. The main therapeutic fields are in oncology, cardiovascular, gastro-intestinal and neurodegenerative diseases.

3. Findings from the survey

Awareness of the program

The first question sought feedback on the general level of awareness of the SME regulation and its implementing measures.

The majority of respondents (77%) indicated that they were aware of the agency's SME programme with 50% rating it 'to some extent' and 27% 'to a great extent'.

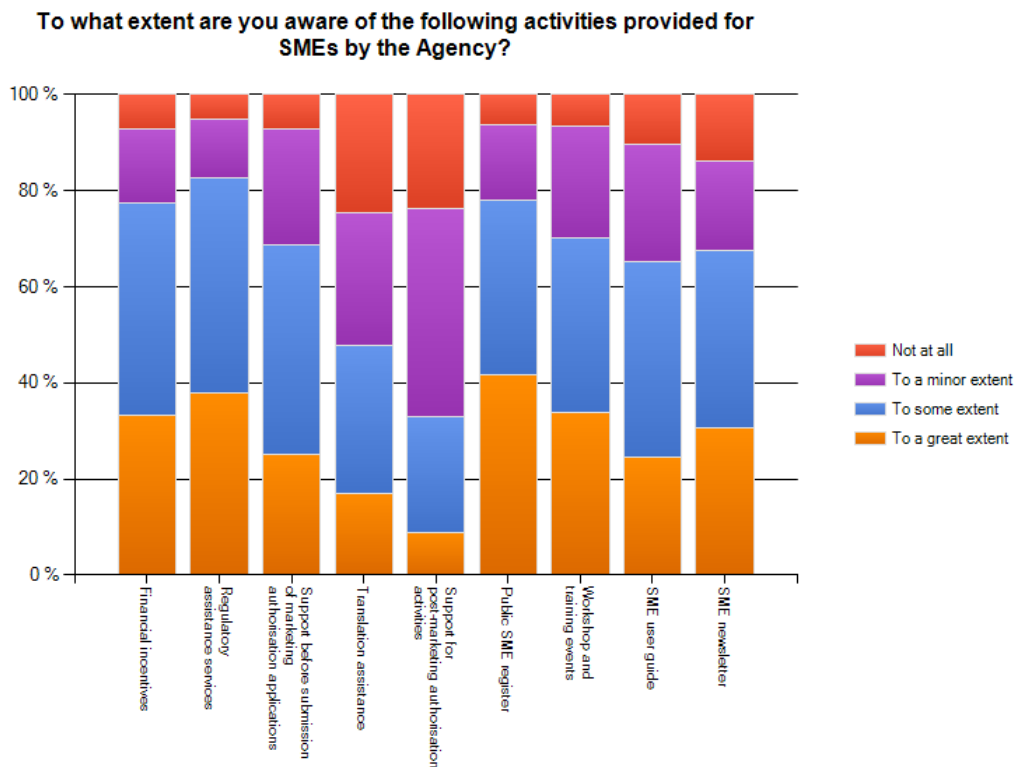


Feedback on the respondents' knowledge of the various specific incentives was also requested. These included the following:

- Financial incentives
- Regulatory assistance

- Support before submission of marketing authorisation application
- Translation assistance
- Support for post-marketing authorisation activities
- Public SME register
- Workshop and training events
- SME user guide
- SME newsletter

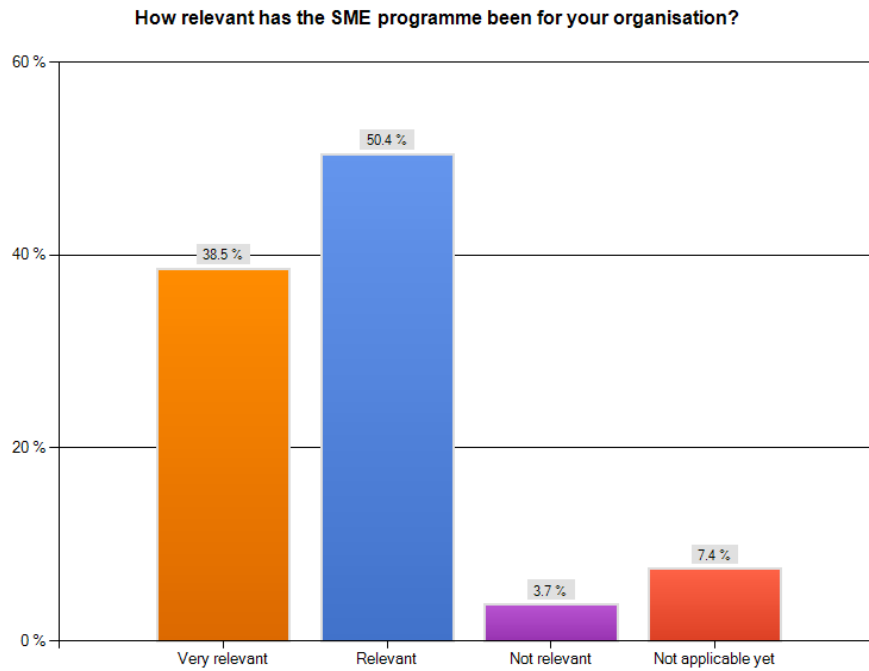
The measure which scored the highest was regulatory assistance (to a great extent 37.9%, to some extent 44.6%), followed by the SME register (to a great extent 41.5%, to some extent 36.4%), and the financial incentives (to a great extent 33.3%, to some extent 44.1%), with the lowest being ‘support relating to post-marketing authorisation activities’ (43.6% rated the awareness as ‘minor’). The low score for post authorisation support should be seen in the context that the majority of SMEs which are currently registered with the EMA are development stage companies yet to place a product on the market. Furthermore, the focus of the SME regulation is on the main financial and administrative entry hurdles pre-marketing authorisation.



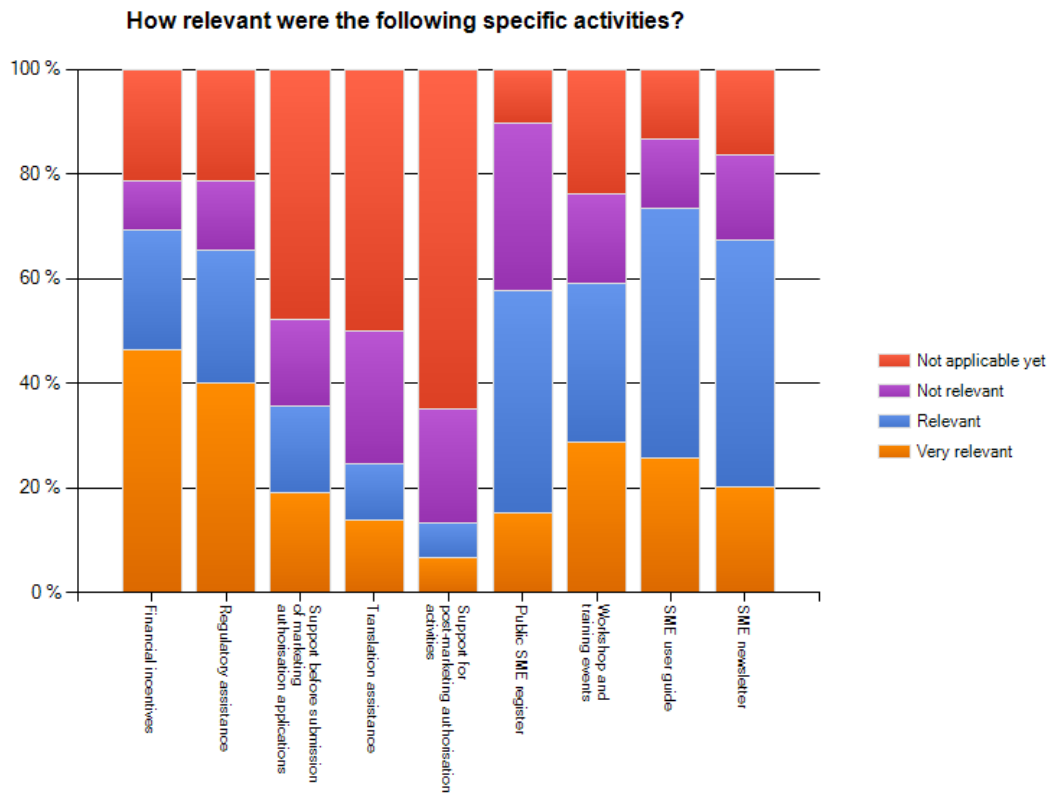
Relevance of the program

Questions on the relevance of the SME programme were filtered only to those companies which applied and received SME status from the EMA and had benefitted from the incentives (135 responses).

A high proportion of respondents indicated that the SME initiative had been relevant or very relevant to their company.



The breakdown into the specific support measures/activities is provided in the following chart:

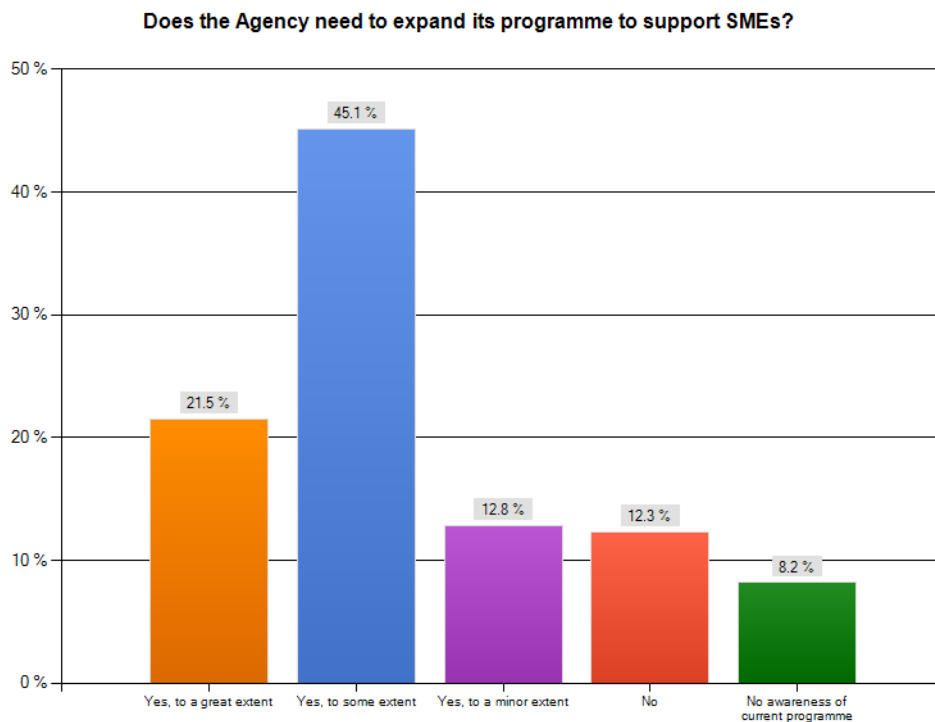


In terms of relevance, the SME user guide rated the highest (very relevant 25.8%, relevant 47.5%) followed by the financial incentives (very relevant 46.5%, relevant 22.8%), the SME newsletter (very relevant 20.3%, relevant 47.2%) and regulatory assistance (very relevant 40.2%; relevant 25.2%), the workshops and training events (very relevant 28.7%, relevant 30.3%) and the public SME register (very relevant 15.2%, relevant 42.4%). The support before submission of the marketing authorisation application, translation assistance and the support for post-authorisation activities were not applicable yet for 48%, 50% and 65% respectively. As noted earlier, many of the registered companies are still at a relatively early stage of development. The financial incentives scored lower for veterinary respondents (very relevant 34.2%, relevant 18.8%).

Scope of the program

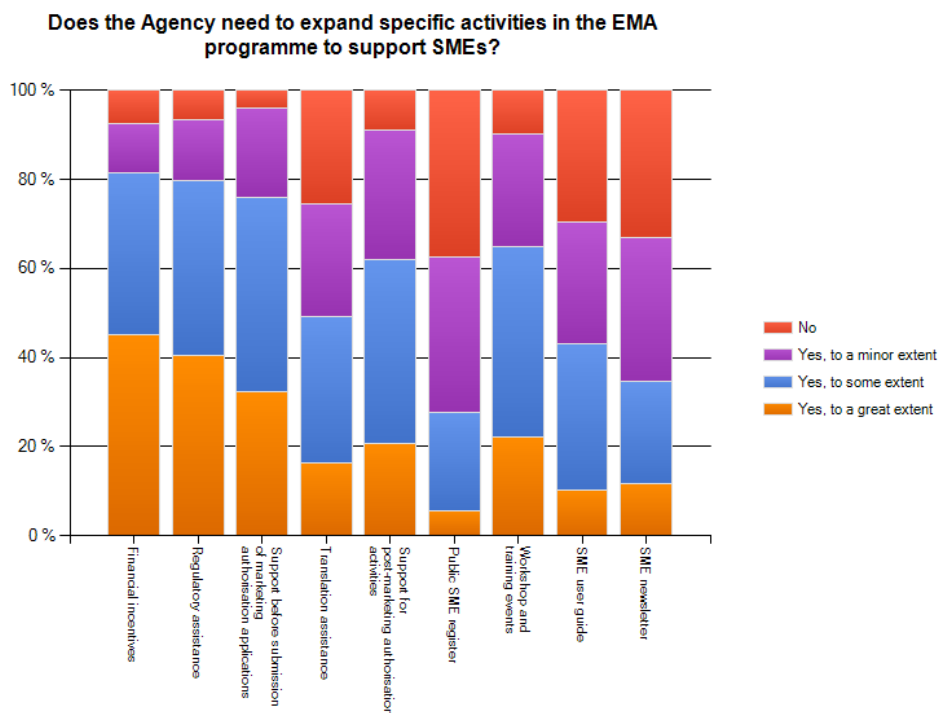
The questionnaire went on to request comments on the extent to which the measures had addressed the needs of SMEs and whether particular aspects might need reinforcing.

Overall the respondents are generally satisfied with the scope of the program. Twelve percent (12%) of respondents consider that the current programme is sufficient, 12% that minor changes are needed, and 45% that it needs expanding 'to some extent'. Only 21% considered that the programme needs to be expanded 'to a great extent'.



Looking at the specific measures, a majority of respondents considered that the Agency should significantly extend its financial incentives (to a great extent 45%, to some extent 36%) followed by regulatory assistance (to a great extent 40%, to some extent 39%), pre-authorisation regulatory support (to a great extent 32%, to some extent 43%), workshops/training events (to a great extent 22%, to some extent 43%), and post-authorisation regulatory support (to a great extent 20%, to some extent 41%). The translation assistance and SME User guide considered as activities to be expanded to 'some extent'.

There were limited suggestions to further develop the SME register (37%) and SME Newsletters (33%).

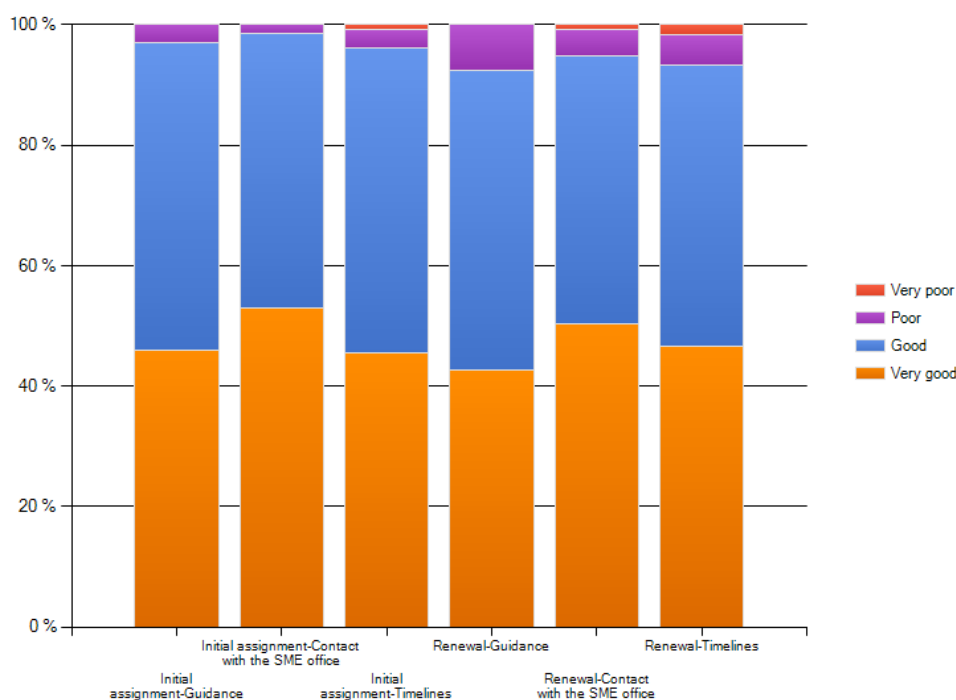


Feedback on the SME registration

The survey also took the opportunity to receive comments on the process for registration as an SME that companies have to apply for before benefitting from the incentives.

The level of satisfaction of respondents with SME assignment process was very high, 90% of SMEs were satisfied with the overall process of registration with SME office. Details about the initial assignment and renewal process are provided in the following chart:

How good was the Agency's SME registration process?



A small number of companies (7%) considered that the SME renewal process would benefit from improved guidelines and timelines.

4. Challenges and suggestions for the future

Respondents were asked to provide comments on the issues they presently face and those that they would consider as emerging ones within the next 5 years and comment on measures to address these challenges in the future. One hundred and twenty-five (125) responses were received. There were common themes in the responses provided and they have been grouped in this report.

4.1. Theme: Funding and finance

Challenges identified in survey	Suggested actions from respondents
<ul style="list-style-type: none"> • Diminishing access to early seed capital for start-ups • The high research and development costs in particular the increase of clinical trials costs and its financing. • Unstable financial environment and constraints to access to capital to recruit qualified people and fund research • Lack of public funding for translational clinical research 	<ul style="list-style-type: none"> • Increase interaction between credit institutions and SMEs to improve access to funds • Increase funding targeted at SMEs in future framework programs

<ul style="list-style-type: none"> • Requirements for EU funding e.g. supporting consortia vs. individual companies • Increasing competition from third countries (e.g. China in particular for biotech products) • Finding partners and nurturing collaborations • Attracting and managing limited in-house qualified scientific and regulatory expertise e.g. for paediatrics related issues. 	
---	--

4.2. Theme: Regulatory

Challenges identified in survey	Suggested actions from respondents
<ul style="list-style-type: none"> • Increasing initial and post-authorisation regulatory requirements and their impact on technical and regulatory manpower needed to prepare multiple 'similar' administrative dossiers for multiple regulatory authorities and procedures at National/EU/International level. • Length of regulatory process in particular for generics • High premarketing applications costs • Implementation of e-CTD/e-submissions and concern over increased electronic reporting to databases • Concern over health technology assessments, changes in pricing reimbursement environment indicating a lack to support to innovation. • High post-marketing costs of regulatory activities (e.g. financial burden of variations regulation, MedDra, product information maintenance in multiple languages) and the cost of remaining on the market for niche products. 	<ul style="list-style-type: none"> • Simplify regulation, the registration process and the need for multiple regulatory documents e.g. development of a common regulatory document for multiple applications to CHMP, CAT, PDCO, COMP and NCAs. • Speed up the regulatory process (in particular for generics) • Extend the scope of fee incentives (e.g. complete waiver for scientific advice; MAA fee reduction vs. deferrals; introduce fees connected to sales by instalments; match the annual fee with the revenues in the first couple of years after approval until reimbursement) • Increase support to SMEs during compilation and dossier preparation • Facilitate the use of e-submissions through an electronic gateway and make electronic submissions mandatory throughout the EU • Use tools such as conditional marketing authorisation, accelerated assessment, deferrals of PIP and rolling review more effectively

4.3. Theme: Scientific advice

Challenges identified in survey	Suggested actions from respondents
<ul style="list-style-type: none"> Lack of guidance (or insufficiently detailed) in many therapeutic fields, for new highly innovative category of products (e.g. personalised medicines, advanced therapies, companion diagnostics or new methodologies in clinical trials). Increasing demands and complexity of regulatory requirements with impact on the length and cost of developments Lack of understanding of requirements e.g. paediatric requirements, QTc studies 	<ul style="list-style-type: none"> Develop science based guidance in emerging fields (e.g. white papers, reflection papers, newsletters) and consider impact assessment of new regulatory guidance Further harmonise regulatory requirements Develop more, informal, faster, pre- and post-scientific advice Further develop the support to global development plans to increase efficiency of the drug development and the global acceptance of dossiers

4.4. Theme: Information and communication

Challenges identified in survey	Suggested actions from respondents
<ul style="list-style-type: none"> Lack of information about changing regulatory requirements and legislation Understanding the regulatory review process and its complexity Understanding of SME services available from EMA. Difficulty in finding partnerships, patients in clinical trials in particular for orphan diseases, and expertise 	<ul style="list-style-type: none"> Increase communication, transparency, assistance and information e.g. overview of regulations (EU, MS etc), fees structure for post authorisation activities, file requirements Propose more opportunities for free education (case studies, interactive training, webinars, training workshops) Networking platforms to help SMEs to develop partnerships with academia and investors

4.5. Theme: Regulatory authorities

Challenges identified in survey	Suggestions from respondents
<ul style="list-style-type: none"> Lack of SME support structures (regulatory advice, economic incentives) at national level. Remaining regulatory differences between EU countries in particular regarding clinical trials Lack or insufficient support to regulatory 	<ul style="list-style-type: none"> Introduce incentives to support to SMEs at national level and establish collaborations between European and national structures. Need for further harmonisation of regulations between agencies including the streamlining of CTA/ethics authorisation system

authorities in developing countries	<ul style="list-style-type: none">• Support regulatory capacity building in developing countries authorities
-------------------------------------	--

5. Conclusions from the survey

The survey confirmed that, thus far, the initiative has met its intended objectives as the majority of registered SMEs which benefitted from the incentives considered the implementation of the SME Regulation as relevant.

About 26% of respondents had limited knowledge of the SME incentives so there is scope to further increase the information available on the scheme.

The benefits considered the most significant were the SME User Guide, the financial incentives and regulatory assistance. The lower responses rates for support before submission of marketing authorisation applications, support for post-marketing and translation assistance were confounded by the fact that most registered SMEs are development stage companies for which these incentives are not yet relevant.

The financial incentives and regulatory assistance were also considered as areas which should be expanded the most.

The following proposals were suggested as points to consider in future actions and initiatives:

- Access to finance and capital scarcity was a recurring concern expressed. These remarks were made in conjunction with comments on the increasing cost of regulation and its impact on cost and length of drug development.
- The complexity and cost of regulation was frequently raised as a challenge by SMEs; costs linked to the development programme itself, the preparation of multiple regulatory dossiers, and the application fees for regulatory procedures. SMEs considered the EMA fees to be too high and expressed the wish that incentives for pre/post registration are expanded e.g. introduce fee reductions for registration or stagger the payment over longer periods. There was also a desire to introduce similar measures at national level.
- SMEs called for more assistance to be provided during dossier preparation, fee incentives for MAA to be reinforced and a more rapid and simplified processes for the review. Calls to make full use of regulatory approval tools such as conditional approval and rolling review process were expressed and as well as easing of the constraints of the paediatric regulation on developments.
- Suggestions to develop a common European regulatory document to reduce the administrative burden of multiple dossier preparation were made.
- Scientific advice was considered of significant importance to SMEs both in the form of formal scientific advice on specific developments and the availability of scientific guidance in new areas. There were some requests for more, informal, faster, pre- and post-scientific advice. Calls for more impact assessment of regulatory guidance and expanding the advice on global development programmes were also expressed.
- Communication and access to updated information on rules and regulations was a particular concern in light of the escalating number of regulatory requirements that need to be complied with. Suggested actions included the reinforcement of training programs for companies and to further increase exposure to regulatory matters through targeted communications in scientific

areas of interest. Encouraging collaborations and partnering between SMEs, academia and investors through networking platforms was considered as an important tool for communication.

- Having open and wilful authorities which provide assistance and facilitate interactions with SMEs was considered of importance. There were wishes expressed to reinforce the capacity offered by the SME office and develop bridges with national and international structures including developing countries.